Wnt-Dependent Epithelial Transitions Drive Pharyngeal Pouch Formation.

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Public Summary:
Using cutting-edge time-lapse photography, University of Southern California (USC) researchers have discovered clues to the development of the head at the cellular level, which could point scientists to a better understanding of how organs and birth defects form in humans. A team of researchers at the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC has for the first time determined the role of two important molecular signaling pathways that help control the number and position of repeated units of cells that pattern the head and face. Two members of a "Wnt" signaling pathway are instrumental in forming pharyngeal pouches that organize the structure of the head and face. Problems with forming the pouches can result in birth defects, including the rare DiGeorge syndrome, which causes an array of symptoms including an abnormal facial appearance, cleft palate, congenital heart disease, and loss of the thyroid and thymus.

Scientific Abstract:
The pharyngeal pouches, which form by budding of the foregut endoderm, are essential for segmentation of the vertebrate face. To date, the cellular mechanism and segmental nature of such budding have remained elusive. Here, we find that Wnt11r and Wnt4a from the head mesoderm and ectoderm, respectively, play distinct roles in the segmental formation of pouches in zebrafish. Time-lapse microscopy, combined with mutant and tissue-specific transgenic experiments, reveal requirements of Wnt signaling in two phases of endodermal epithelial transitions. Initially, Wnt11r and Rac1 destabilize the endodermal epithelium to promote the lateral movement of pouch-forming cells. Next, Wnt4a and Cdc42 signaling induce the rearrangement of maturing pouch cells into bilayers through junctional localization of the Alcama immunoglobulin-domain protein, which functions to restabilize adherens junctions. We propose that this dynamic control of epithelial morphology by Wnt signaling may be a common theme for the budding of organ anlagen from the endoderm.